

REMARKS

I. Status

No claims are amended. Claims 1, 3-8, 12-16, and 34-35 remain pending. A claim listing has been included for the convenience of the Office.

II. Response to Rejections

A. Obviousness Rejections

Claims 1, 3-8, and 12-16 stand rejected as being allegedly obvious in view of the three-way combination of Calvin (U.S. Patent No. 5,098,843), Mehta (U.S. Patent No. 6,122,599), and Torr (U.S. Patent No. 6,891,712). Applicant respectfully disagrees and requests favorable reconsideration.

1. Effecting Electroporation While An Electric Field Is Constant Is Not Obvious

Independent claim 1 involves *effecting electroporation while the electric field is substantially constant* in terms of magnitude and wherein *a polarity of the electric field is periodically reversed*. Independent claim 7 involves displacing a pair of electrodes and a sample relative to one other *while the electric field is substantially constant* in terms of magnitude so that the sample is displaced across electric field lines *for a time sufficient to effect electroporation* wherein *a polarity of the electric field is periodically reversed*.

These features are not taught or suggested by the cited art, alone or in combination.

1. Effecting Electroporation While An Electric Field Is Constant Is Not Obvious

The Office alleges that, of the three references, Calvin is the one that teaches effecting electroporation *while an electric field is substantially constant*. See Office Action, pages 2-3. Calvin, however, explicitly does not stand for this proposition. In fact, none of the references

teach or suggest this feature, nor is this serious and significant gap in the art anywhere shown to be obvious.

In Calvin, electroporation is only effected through use of an electric field specifically and purposefully designed to not be substantially constant. *See* Calvin, column 8, lines 20-41. In particular, Calvin explains that over a distance b' , the distance between electrodes remains nearly the same, resulting in an electric field strength of about 12,000 volts/cm. *See* Calvin, column 8, lines 20-28. Over the distance b'' , however, “*the electric field strength ... falls off greatly* as such electrodes diverge.” *See* Calvin, column 8, lines 28-35. In Calvin, electroporation is effected over the combined distance $b' + b''$ because it is over this distance that a specific electroporation electric pulse characteristic of a different embodiment is simulated. *See* Calvin, column 8, lines 35-41.

Accordingly, in Calvin, electroporation is not effected while an electric field is substantially constant, as claimed. Instead, in Calvin, electroporation is done only according to an electric field whose field strength “falls off greatly” during the electroporation. Calvin not only fails to disclose or suggest effecting electroporation with a substantially constant electric field, but it actually *teaches away* from this technique by explicitly requiring electroporation to be effected using an electric field strength that *falls off greatly* in a particular manner. Calvin therefore does not support an obviousness rejection. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007) (discussing principle of “teaching away”). Rather, the fact that the elements of the present invention work together in an unexpected and fruitful manner (effecting electroporation despite the absence of a varying field as taught by Calvin) supports the conclusion that the present design would not have been obvious to those skilled in the art. *Id.*

Applicant notes that the citation of Torr, specifically Torr at column 5, lines 31-37, does not affect the patentability of the present claims nor the arguments presented above. The cited passage of Torr simply states that divergence or convergence of electric field lines can be achieved with curved electrodes. This basic physical truth does not affect the fact that Calvin teaches that one should use a *non-constant electric field for electroporation*. Mehta, likewise, does not affect the arguments raised above since it was relied on only with respect to polarity reversal, which Applicant will now discuss.

2. Electroporation Wherein a Polarity of the Electric Field is Periodically Reversed Is Not Obvious

Claims 1 and 7 involve electroporation wherein a polarity of the electric field is periodically reversed. The Office previously noted that this feature was allowable but now includes the Mehta reference in an attempt to establish its obviousness. Applicant respectfully disagrees.

The *KSR* decision recognizes that obviousness involves a determination of whether there was an “apparent reason” to combine known elements. *KSR*, 127 S. Ct. at 1740-1741. Here, there is no apparent reason to combine Mehta with either of the other references to arrive techniques for electroporation wherein a polarity of an electric field is periodically reversed. Mehta discusses polarity reversal applied to electrodes “to distinguish a signal from the noise” of a specific “passive” electrode that is not an electroporation electrode. *See* Mehta, column 7, lines 30-39). In a different embodiment, Mehta later discloses that one of its apparatuses may further include an electroporation device. *See* Mehta, column 20, lines 31-43. Nowhere here does Mehta mention, use, or suggest polarity reversal as presently claimed. No apparent reason has been shown to combine electroporation polarity reversal with techniques of Calvin (or, even less

so, to the disparate techniques of Torr) using the isolated passage in Torr directed to distinguishing “a signal from the noise” of a non-electroporation device.

3. There is No Apparent Reason To Combine the Cited References

As stated above, establishing obviousness still, after *KSR*, involves showing an apparent reason to combine art. Here, that has not been done. Torr is directed to a disparate “field converter” while Mehta is cited for a passage involving polarity reversal of a different type of electrode on a different type of device to distinguish signal from noise. Piecing these references and passages together exhibits an improper hindsight analysis, which the Supreme Court has explicitly warned against. *KSR*, 127 S. Ct. at 1742 (“A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning.”). As the Federal Circuit has very recently taught, a flexible Teaching, Suggestion, Motivation (“TSM”) test “remains the *primary guarantor* against a non-statutory hindsight analysis.” *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, No. 2007-1223, slip op. at 11 (Fed. Cir. Mar. 31, 2008) (emphasis added). Here, no teaching, suggestion, or motivation has been, nor could be, established to combine the references and passages currently used in support of the obviousness rejections.

B. Conclusion Regarding Obviousness

The cited art, taken alone or in any combination, fails to teach or suggest at least the feature of effecting electroporation while an electric is substantially constant in terms of magnitude. In fact, Calvin teaches away from this principle. Nor has this serious and significant “gap” in the art been shown, in any manner, to be obvious. For this reason alone, the claims are currently allowable. Further, the art does not render obvious the claimed combinations involving polarity reversal. Still further, there has been shown no apparent reason (nor a teaching,

suggestion, or motivation) to combine the cited art in the manner argued by the Office. Rather, the combinations appear to have been based on an improper hindsight analysis.

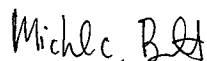
C. Claims 34 and 35

Claims 34 and 35 were added in the previous response and recited features originally present in now-canceled claims 9 and 10, which were found to contain allowable subject matter. *See* Office Action dated March 9, 2007. Applicants note that no rejections have been argued against these claims in the present Action and that these claims remain allowable.

D. Conclusion

Applicant believes this response addresses each rejection and requests favorable reconsideration. The Examiner is invited to contact the undersigned attorney by phone at 512-536-3018 or by e-mail at mbarrett@fulbright.com with any questions.

Respectfully submitted,



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